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The correlation between cardiac troponin I land ischemic stroke severity using the national institutes of health stroke scale

Cardiac troponin I level and ischemic stroke severity in acute ischemic stroke patients

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Abstract
Aim: The aim of this study is to explore the correlation between cardiac troponin I (cTnI) levels and the National Institutes of Health Stroke Scale (NIHSS) in acute ischemic stroke (AIS) patients as well as to determine the significance of cTnI levels in predicting the prognosis of AIS patients.
Material and Methods: A retrospective analysis was conducted on patients diagnosed with AIS who presented to the Emergency Department of Ankara Dışkapı Yıldırım Beyazıt Research and Training hospital between February and June 2018 and had their cTnI levels assessed. Both the cTnI levels and NIHSS scores of these patients were documented.
Results: A total of 151 patients were evaluated. The mortality rate for patients with normal cTnI levels was 1.69% (2 out of 118 patients), while those with elevated cTnI levels had a mortality rate of 32.25% (p=0.001). Of those with normal cTnI levels, 10.92% required intensive care unit (ICU) admission, compared to 40.62% with elevated cTnI levels (p=0.002). The average NIHSS scores for patients with normal and high cTnI levels were 5.83±5.80 and 12.56±7.55, respectively.
Discussion: The results of this study indicate that elevated cTnI levels in AIS patients are associated with a worse prognosis, higher necessity for ICU admission, and increased mortality rates. It is believed that evaluating cTnI levels, a readily available test in AIS patients, will guide clinicians in assessing the patient's prognosis.

Keywords
Stroke, Cardiac Troponin I, National Institutes of Health Stroke Scale

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Introduction

A stroke is defined as a vascular-origin, sudden-onset neurological disorder, which is either focal or global, lasting for more than 24 hours or resulting in death within this period. Stroke ranks as the second leading cause of death globally [1,2]. 87% of all strokes result from ischemia, 10% from an intracerebral haemorrhage, and 3% from subarachnoid haemorrhage [2,3]. Furthermore, stroke stands as one of the predominant causes of disability. Rehabilitation of these patients demands substantial time and resource allocation. As a result, numerous assessment tests have been developed to identify factors predicting post-stroke functional recovery. Among these, the National Institutes of Health Stroke Scale [NIHSS] is one of the most commonly used neurological severity scales.

Cardiac troponin I (cTnI) typically indicates myocardial cell damage and is the gold standard for diagnosing acute myocardial infarction (AMI). However, elevated cTnI can also occur due to non-coronary artery disease causes. Numerous studies have identified elevated cTnI in some acute stroke patients, even in the absence of any cardiac symptoms, and this elevation has been correlated with patient prognosis [4].

In patients with acute ischemic stroke (AIS), electrocardiographic alterations along with troponin [Tn] elevation are not uncommon. Yet, it remains unclear whether this is due to cardiac complications or neural-mediated myocyte damage [5]. Both stroke and AMI share similar risk factors and pathological mechanisms. Consequently, patients with AIS have a higher prevalence of concurrent coronary artery disease, which results in an increased risk of death, paralleling a higher risk of ischemic stroke development [5].

The purpose of this study is to investigate the relationship between serum cTnI levels and the severity of ischemic stroke, as determined by the NIHSS score, in AIS patients. Additionally, this research aims to evaluate the role of cTnI in predicting the prognosis of AIS patients.

Material and Methods

Following approval from the local ethics committee of the Ankara Diskapi Yildirim Beyazit Research and Training Hospital (2018/49-13), a retrospective examination was conducted on 151 patients who presented to the Emergency Department (ED) of the hospital between February and June 2018 and were diagnosed with AIS.

The demographic characteristics and serum cTnI levels of these patients were assessed, and their NIHSS scores were calculated. Exclusion criteria were patients below 18 years of age, those presenting to the ES with disease onset greater than 3 days, patients concurrently experiencing acute myocardial infarction with ischemic stroke, those for whom cTnI tests were not conducted, and individuals exhibiting elevated cTnI levels due to other potential causes such as chronic heart failure, severe liver and kidney failure, severe infection, muscular diseases, tumors, and immune system disorders.

Venous Serum cTnI levels were measured in the biochemistry laboratory using the Beckman Coulter Access 2 device (USA) and the Access TnI kit (USA).

The National Institutes of Health Stroke Scale (NIHSS) was used to quantify clinical findings. The NIHSS serves as a scale to assess neurological functions in AIS patients and provides insights into long-term prognosis. The score employs a point system ranging from 0 to 42. The primary five parameters evaluated are consciousness level, visual assessment, motor functions, sensory neglect, and cerebellar functions [3]. Baseline neurological status in the NIHSS is categorized as follows: normal/near-normal examination (0 points), mild stroke (1-4 points), moderate stroke (5-14 points), moderate/severe stroke (15-20 points), and severe stroke (>20 points). Furthermore, the NIHSS scoring system also predicts patient prognosis [6]. A good prognosis is assessed as 0-6 points, a moderate prognosis as 7-15 points, and a poor prognosis as 16-42 points [7].

Statistical Analysis

Data analyses were carried out using SPSS (Statistical Package for Social Sciences) version 11.5 for Windows. Descriptive statistics for continuous data were provided as mean ± standard deviation or median (minimum-maximum), depending on the normality of the distribution. For categorical variables, data were presented as frequency (percentage). For comparisons of continuous variables across two or more groups, the Mann-Whitney U or Kruskal-Wallis tests were employed. For categorical variables, the Chi-square or Fisher's Exact test was utilized. Relationships between continuous variables were assessed using the Spearman correlation coefficient. For all statistical analyses conducted, the significance level was set at α=0.05.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

Out of the 151 patients included in the study, 76 were female, accounting for 50.3% of the sample. The age of the patients ranged from 36 to 96, with a median age of 74 (IQR 25-75).

The serum cTnI levels of the patients varied between 0 and 3.64 ng/ml. The mean cTnI value was 0.11 ± 0.47 ng/ml, and the median value was 0.01 ng/ml. A total of 119 patients had cTnI levels within the normal range (78.8%), whereas 32 patients exhibited elevated levels (21.2%). The recognized normal range for cTnI was 0-0.04 ng/ml.

For the patients studied, the NIHSS scores varied between 0 and 29, with a median score of 5 (IQR25-75) (2-10).

Patients with normal cTnI levels had an average NIHSS score of 5.83±5.80, whereas those with elevated cTnI levels had an average score of 12.56±7.55. A statistically significant relationship was identified between cTnI levels and NIHSS scores (p=0.001). The correlation between cTnI and NIHSS scores was found to be significant, though it was a weak correlation (p=0.002), with a correlation coefficient (r) of 0.254. The NIHSS score was found to be significantly higher in patients with AF (p=0.001). Of the 151 patients included in the study, 137 were discharged, while 12 patients passed away during their hospitalization. The outcomes of 2 patients remained unknown due to missing records.

Upon evaluating the relationship between the outcomes during hospitalization and cTnI levels, we observed a statistically significant higher mortality rate in patients with elevated cTnI (p=0.001) (Table 1).

Table 1. Correlation between cardiac troponin I level and mortality.

	Number of patients (n) (%)			p-value
	Discharged	Exitus	Total	
Normal	116 (%77.9)	2 (%1.3)	118 (%79.2)	
High	21 (%14.1)	10 (%6.7)	31 (%20.8)	0.001
Total	137 (%91.9)	12 (%8.1)	149 (%100)	

* Outcomes of 2 patients remained unknown due to missing records.

Table 3. Correlation between the National Institutes of Health Stroke Scale and admission location.

Admission Location	Average NIHSS Value ± SD
Discharged from ED	3.81 ± 4.91
Neurology Ward	5.12 ± 4.26
Intensive Care Unit	17.84 ± 5.93
Referred to an External Center	17± 0.00

NIHSS: National Institutes of Health Stroke, ED; * Emergency Department.

Table 2. Association between cardiac troponin I levels and admission location.

Cardiac troponin I level	Discharged from ED	Neurology Ward	Intensive Care Unit	Referred to External Centre	Total	p-value*
Normal	14 (%9.3)	91 (%60.3)	13 (%8.6)	1 (%0.7)	119 (%78.8)	
High	2 (%1.3)	17 (%11.3)	13 (%8.6)	0 (%0)	32 (%21.2)	0.002
Total	16 (%10.6)	108 (%71.5)	26 (%17.2)	1 (%0.7)	151 (%100)	

ED; Emergency Department, * Comparing ward admissions to intensive care unit admissions

The admission locations of the patients were compared with their cTnI levels. When comparing general ward admissions to intensive care unit (ICU) admissions, elevated cTnI values were observed in 15.7% of the patients admitted to the general ward, whereas 50% of those requiring ICU monitoring had raised cTnI levels. We found this difference to be statistically significant (p=0.002) (Table 2).

There was no statistically significant difference between elevated cTnI levels, and the duration of hospital stay for the patients (p=0.701).

There was a statistically significant difference in NIHSS scores between patients discharged from the ED and those requiring intensive care, as well as between patients requiring ward admission and those needing intensive care (p=0.001). However, there was no statistically significant difference in NIHSS scores between patients discharged from the ED and those admitted to the ward (p=0.588) (Table 3).

The correlation between NIHSS score values and mortality was statistically significant (p=0.001). In patients who were discharged in recovered condition the average NIHSS score value was 6.01 ± 5.65, whereas exitus was 19.75 ± 4.71.

Discussion

Our study highlighted two significant findings. Primarily, AIS patients with elevated cTnI levels demonstrated a higher in-hospital mortality rate compared to those with normal cTnI levels. Secondly, our study indicates a correlation between elevated cTnI levels and an increased need for intensive care in AIS patients. Both outcomes converge on the understanding that elevated serum cTnI in AIS patients is associated with a poorer prognosis.

The mechanism behind elevated cTnI in AIS patients remains incompletely elucidated, although it is believed to be different from that in acute coronary syndromes [5,8,9]. Haumer et al. reported that stroke patients with elevated cTnI have a correlation with increased neutrophil counts, suggesting that a robust inflammatory response could induce myocardial damage [10]. Recent studies suggest that the rise in cTnI during a stroke could be attributed to mechanisms similar to stress-mediated myocardial supply-demand mismatch (akin to Takotsubo cardiomyopathy) [11]. Enhanced sympathetic activity secondary to insular cortical damage, imbalances between sympathetic and parasympathetic systems, and relative shifts in adrenaline and cortisol levels might contribute to myocardial damage and a subsequent rise in cTnI [12,13,14]. Yıldız et al. observed that ischemia in cerebral regions supplied by the anterior circulation showed a higher cTnI elevation compared to other brain regions. Evaluations of electrocardiography in these patients revealed changes suggestive of myocardial ischemia, proposing that elevated cTnI in AIS might be attributable to an accompanying acute coronary syndrome [12]. Elevated levels of CTnI were found in approximately 5-10% of AIS patients [9]. It was noted that an average of 18.1% of AIS patients exhibit elevated cTnI, with rates ranging from 0% to 34% across studies [15]. In this study, elevated cTnI values were identified in 21.2% of the patients.

A statistically significant correlation was identified between cTnI values and NIHSS scores in this study. Similarly, in a study by Cui et al., ischemic stroke patients with elevated cTnI levels were found to have higher NIHSS scores compared to those with normal cTnI levels [4]. In a study by Budincevic et al. on 198 AIS patients evaluating the impact of cTnI values on patient outcomes, the relationship between patients' cTnI values and their mRS scores at discharge was examined. It was found that patients with increased cTnI values had higher mRS scores compared to those with normal levels [16]. Cui et al.'s study showed that elevated cTnI in AIS patients did not influence their hospital stay duration [4]. Similarly, in this study, a statistically significant correlation was not observed between elevated cTnI levels, and the number of days patients spent in the hospital.

In a study conducted by Yıldız et al., they evaluated a group of patients admitted to the hospital due to acute coronary syndrome and who experienced an AIS during their stay. Their study examined the relationship between cTnI elevation and the

disease prognosis in these patients, which indicated a cTnI level of 20 ng/mL and above as an independent risk factor concerning mortality. However, when evaluating AIS patients based on NIHSS scores and assessing patients' dependency through mRS, they did not find a statistically significant difference between patients with normal and elevated cTnI values. Furthermore, it was suggested that regarding the increase in mortality could be attributed to an acute coronary syndrome concurrent with AIS [12]. Data analysis of our study concluded that elevated cTnI levels are associated with increased mortality and higher NIHSS scores, indicating a more severe clinical course. It is believed that the difference between the findings of the two studies might be explained by the dissimilarity in the patient groups under consideration.

In the study by Budincevic et al., elevated cTnI values were associated with increased in-hospital mortality [16]. Upon evaluating our study, it was observed that patients with high cTnI levels had a statistically significant increase in in-hospital mortality rates. Additionally, it was determined that patients with elevated cTnI values also presented with higher NIHSS scores.

Another study by Kirkman et al. recommended that patients with an NIHSS score exceeding 17 be monitored in intensive care units [17]. Yaghi et al. emphasized the significance of transthoracic echocardiography during the diagnosis, treatment, and typing stages of AIS patients in their study. Their study identified that post-transthoracic echocardiography management alterations occurred at a higher rate for patients with elevated Tn values than for those with normal values [18]. Similarly, in our research, it was observed that patients requiring intensive care had statistically significantly higher NIHSS scores compared to those requiring ward admission. Moreover, a greater proportion of patients with elevated cTnI values required intensive care. However, the literature revealed no studies evaluating the correlation between cTnI elevation and the requirement for intensive care in AIS patients. It is assumed that this may be due to patients with elevated cTnI levels having a more severe clinical presentation (higher NIHSS scores).

In a study conducted by Chang et al. with 330 patients experiencing their first ischemic stroke, stroke severity was identified as the most potent determinant of hospital stay duration. It was identified that for patients with an NIHSS score below 15 (indicating mild-to-moderate neurological damage), every one-point increase in the score prolonged the hospital stay by approximately one day. Conversely, for patients with scores above 15 (indicating severe neurological damage), each additional point reduced the duration by roughly a day [19]. Appelros's study determined stroke severity via the NIHSS score and then explored the relationship between the NIHSS score and hospital stay duration. Their results revealed that up to an NIHSS score of 19, every one-point increment increased the stay by 0.75 days for acute care and a total of 3.4 days when considering long-term rehabilitation. This increment was statistically significant. After exceeding an NIHSS score of 19, the stay duration initially plateaued and then decreased, which they attributed to the number of severe stroke patients challenging to rehabilitate [20]. In our study, a higher mortality rate was observed among patients with elevated NIHSS scores. However, short-term hospital prognoses of AIS patients were specifically evaluated by comparing cTnI values and NIHSS scores. Gajurel et al. compared AIS patients' NIHSS scores with mRS and associated high NIHSS scores with adverse outcomes [7]. In the study by Ducci et al., an NIHSS score exceeding 17 was identified as an independent marker for in-hospital mortality [21]. Similarly, Magdon-Ismail et al. showed that a higher NIHSS score at admission increased mortality over a post-discharge one-year period [22]. Zhao et al. also highlighted the association between elevated NIHSS scores and increased mortality [23].

Conclusion

Our study concluded that in patients with AIS, elevated cTnI levels are associated with a poorer prognosis, increased need for intensive care, and higher in-hospital mortality rates. It is believed that assessing cTnI values, a readily accessible test for AIS patients, will provide clinicians with valuable guidance in evaluating patient prognosis. We emphasize the significance of closely monitoring patients with high cTnI values during their hospital stay. Anticipating higher morbidity and mortality rates in these patients and subsequently implementing preventative measures may positively influence their prognosis.

Limitations

Limitations of the study include the single-center design and retrospective nature.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest

The authors declare no conflict of interest.

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